REMARKS

Claims 56 to 68 have been cancelled. New claims 82-91 have been submitted. Support for new claims 82-91 is found in the specification as filed on page 5 at line 28 to page 6 at line 6, on page 13 at lines 1-6 and 12-13, on page 19 at lines 10-12, and on page 20 in Table I.

Applicants thank the Examiner for withdrawing outstanding claim rejections under 35 USC §112, first paragraph. Applicants thank the Examiner for entering the Substitute Sequence Listing and amendments to the specification filed on September 22, 2003.

Regarding rejections of claims

Claims 69-92 are currently pending. Claims 56-81 have been rejected. Claims 56-68 have been cancelled, rendering rejection of Claims 56-68 moot. Therefore, Claims 69-81 currently stand rejected. Applicants request consideration of the following remarks concerning the outstanding claim rejections.

Double patenting rejections

Claims 69-81 stand rejected for obviousness-type double patenting as being allegedly upatentable over claims 1-9 of Patent No. 5,817,629. Applicants respectfully request that the obviousness-type double patenting rejections be held in abeyance until allowable subject matter has been indicated, at which time a terminal disclaimer will be filed. The filing of the terminal disclaimer is in order to further prosecution of the subject application and is not to be construed as acquiescing to the propriety of the rejection.

Rejections under 35 U.S.C. §103

Claims 69-81 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Hafler *et al.* (US Patent No 5,571,500) in view of Martin *et al.* (*J Immunol.* 1990 145:540-548) or Ota *et al.* (*Nature* 1990 346:183-187).

In the Office Action mailed June 17, 2003 (Final OA), it was stated that it would have been obvious "to substitute the fragments of MBP in the method of treating MS taught by Hafler *et al.* with the characterized immune reactive fragments of MPB taught by Martin *et al.* and Ota *et al.*" (Final OA, Section 8, page 8). It was further alleged that one of ordinary skill in the art would have been motivated to make the substitution and would have expected success "because

the peptides taught by Martin *et al.* and Ota *et al.* are know[n] to contain the immune reactivity property found in the whole MPB taught by Hafler *et al.*" (Final OA, Section 8, page 8).

In the Advisory Action mailed November 5, 2003, it was stated that "a person of ordinary skill in the art would have been motivated to combine the references and use the fragments of Martin *et al.*and Ota *et al.*in the method of Hafler *et al.*" (Advisory Action, Item 5).

Applicants respectfully traverse.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, the prior art reference, or references when combined, must teach or suggest all the claim limitations. There must be also some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Finally, there must be a reasonable expectation of success. *See*, MPEP §§ 2142, 2143.

In the present case, the references do not teach a method of reducing free anti-myelin basic protein in a patient as recited in Claims 69-81. Further, there is no suggestion or motivation to modify or combine the references teachings in the manner proposed. Additionally, there is no reasonable expectation of success from the proposed combination. Because the basic criteria for a *prima facie* case of obviousness have not been met, rejection of Claims 56-81 under 35 U.S.C. §103 is improper and should be withdrawn.

The cited references do not teach the claimed invention.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. MPEP §2143.03, citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). As noted in the Final Office Action mailed June 17, 2003, "Hafler *et al.* teach the method of administration of autoantigens for the treatment of autoimmune diseases," specifically MBP or fragments. (Final OA Section 8 at page 6). It was further noted that Martin *et al.* teach MBP as a candidate antigen involved in pathogenesis and disclose MBP peptides, and Ota *et al.* teaches MBP peptides and the involvement of these peptides in MS (Final OA Section 8, page 7). Applicants respectfully point out that combining a method of treating MS by administering autoantigens as taught by Hafler *et al.* combined with peptides involved in MS as taught by Martin *et al.* and Ota *et al.*, does not teach reducing free anti myelin basic protein in a patient as in Claims 69.81. Because the cited references do not

teach all the claim limitations of the invention, this criterion for a *prima facie* case of obviousness has not been satisfied. Therefore, the rejection is improper and should be withdrawn.

No suggestion or motivation to combine references to make the claimed invention

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988); *In re Jones* 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). See generally, MPEP §2143, especially §2143.01. In the present case, there is no teaching, suggestion, or motivation to combine or modify the cited references in such a way as to produce the claimed invention.

Applicants traverse the argument put forth in the Office Action that one of ordinary skill in the art would allegedly have been motivated to substitute the fragments of MBP in the method of treating MS taught by Hafler *et al.* with the characterized immune reactive fragments of MBP taught by Martin *et al.* and Ota *et al.* First, such a combination does not even teach the claim limitations of the present invention. Second, Hafler *et al.* neither teach nor suggest nor provide motivation for using peptides such as those disclosed by Martin *et al.* and Ota *et al.* in the method of treating MS by inhalation of autoantigens taught by Hafler *et al.* Not only does Hafler *et al.* do not teach peptides of at least 8 to 25 amino acids contained within SEQ ID NO: 1, but Hafler *et al.* describe an "autoimmune suppressive fragment" as "any peptide or polypeptide containing partial amino acids sequence or moieties of autoantigens and possessing the ability to suppress or prevent an autoimmune response upon aerosol administration." (Hafler *et al.*, col. 5 at lines 14-19). In contrast, Martin *et al.* allegedly teach MBP as a candidate antigen for the autoimmune process important for the pathogenesis of multiple sclerosis (MS), and Ota *et al.* allegedly disclose MBP peptides and the involvement of these peptides in MS. Neither Martin *et al.* nor Ota *et al.* teach or suggest administration of these peptides for treatment of MS.

Not only is there no teaching or suggestion to combine reference, there is no motivation in the references to combine or modify the cited references to produce the invention of Claims 56 to 81. Here, the mere fact that the teaching of immune reactive fragments of MPB disclosed in Martin *et al.* or Ota *et al.* can be combined with the teaching of Hafler *et al.* that autoimmune

suppressive fragments can be administered to treat MS, does not render this combination obvious unelss the references suggest the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Further, the argument that a combination is "obvious to try" is not acceptable for establishing obviousness. *In re Tomlinson* 150 USPQ 623 (CCPA 1966). Finally, absent a suggestion, teaching, or motivation to combine references, such a combination is unacceptable "hindsight" that does not establish a *prima facie* case of obviousness. *In re Dembiczak* 175 F.3d 994, 50 USPQ2d 1614 (Fed. Cir. 1999). Because there is no teaching, suggestion, or motivation for the proposed combination of references, this criterion for establishing a *prima facie* case of obviousness has not been satisfied and the rejection should be withdrawn.

No reasonable expectation of success

Prima facie obviousness also requires a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). In the present case, the combination of cited references not only do not teach the claimed invention, but also provides no reasonable expectation of the success that has been disclosed and claimed in the present application. There is no reasonable expectation that combining the method of administering autoantigens taught by Hafler *et al.*, with one or more peptides taught by Martin *et al.* or Ota *et al.*, would produce the claimed method of reducing free anti-myelin basic protein in a patient (Claims 69-81). In fact, Martin *et al.* and Ota *et al.* would teach away from administering MBP peptides that are involved in MS. Because there is no reasonable expectation of success from the proposed combination of references, this criterion for establishing a *prima facie* case of obviousness has not been satisfied and the rejection should be withdrawn.

CONCLUSION

Claims 56-81 were previously pending. Claims 56-68 have been cancelled and new claims 82-91 have been presented. Claims 69-81 stand rejected. Applicants request that new claims 82-91 entered, and request that Claims 69-81 be reconsidered in light of the remarks presented above.

If the Examiner believes that a telephone interview would expedite prosecution of this application, she is encouraged to telephone the undersigned Applicants' attorney.

The Applicant believes all required fees have been paid. However, if any fees are due in connection with this submission, please charge any such fee or credit any overpayment to Deposit Account No. 50-2212.

Respectfully submitted,

PILLSBURY WINTHROP LLP

Date: December 16, 2003 By: _____
Donna O. Perdue, Ph.D.
Reg. No. 51,166

11682 El Camino Real, Suite 200
San Diego, CA 92130
Tel. No.: (858) 509-4093
Fax No.: (858) 509-4010